REMARKS

Claims 1-3, 6-15, and 19-21 are currently pending. Claims 1, 20 and 21 are the pending independent claims. Claim 21 is new. All of the prior pending claims stand rejected under 35 U.S.C. § 103 over Liu (US 6,875,432) in view of Goldenberg (US 6,432,449) in further view of Sahner (US 6,579,521). Claims 1, 8 and 20 have been amended. No new matter has been introduced by the amendments, which are supported by the disclosure of the original claims and the specification as discussed in more detail below. Support for new claim 21 may be found in paragraph [0043] of Applicants' published disclosure.

Each of the foregoing rejections is respectfully traversed and favorable reconsideration and allowance of the claims are requested in view of the above amendments and following remarks.

I. § 103 Rejection

In paragraph [0185] of Applicants' disclosure, Applicants state the following:

> The inventive pharmaceutical compositions were prepared by dilution of the sterile bulk concentrate of G-CSF with appropriate sterile buffer solutions which were previously filtered through 0.2 PES/Nalgene filter. The final concentrations of G-CSF were 0.3 mg/ml or 0.6 mg/ml, respectively.

Here, the concentration range of G-CSF is given, generally ranging from about 0.3 mg/ml to about 0.96 mg/ml. Claims 1 and 20 have been amended to include this concentration range. Claim 1, as amended, claims, *inter alia*, a stable pharmaceutical composition of granulocyte-colony stimulating factor (G-CSF) comprising a therapeutically effective amount of a non-glycosylated G-CSF in a concentration ranging from about 0.3 mg/ml to about 0.96 mg/ml. Claim 20 has also been amended to contain these same elements.

Applicants respectfully assert that the Examiner's conclusions in the recent Office Action are in error because the combination of Liu, Goldenberg, and Sahner do not teach or otherwise suggest all of the limitations of claims 1 and 20, as amended.

Liu teaches that the field of the invention "pertains to ***concentrated*** protein formulations with ***reduced viscosity***." Liu, Column 1, lines 14-15 (emphasis added). Accordingly, Liu explicitly teaches that the final protein in his formulation has a concentration of at least 40 mg/ml. *See* Liu, Col. 28, line14 – 16. More preferably, Liu's formulation has a final protein concentration of at least 80 mg/ml. *See* Liu, Col. 3, lines 18 – 20. Even Liu's intermediary

compositions (which, importantly, are not the same as Applicants' claimed composition) have a protein concentration of greater than 2 mg/ml. Thus, the protein concentrations taught in Liu are directly contrary to those specified in the current claims.

Like Liu, Goldenberg mentions G-CSF as a protein contemplated by the invention at Column 8, line 37. However, Goldenberg makes little reference to protein concentration, and the only specific example discussing G-CSF (Example 5) discloses a protein concentration of 48.2 mg/ml—within the same range as taught in Liu. Goldenberg makes a very general statement under the "Dosages" heading about the accepted concentration(s) required for a drug as described therein to establish a therapeutic effect (i.e., between 0.10 μg/kg/day to 100 mg/kg/day). This general statement, however, is so broad that it covers virtually any concentration of any medicament used in the industry, and the statement is not a specific teaching or suggestion with respect to any particular protein or active substance disclosed in Goldenberg.

Thus, both Liu and Goldenberg explicitly teach the use of G-CSF at a specific concentration range (i.e., at least about 50 mg/ml, or greater) which is considered "high" and *desirable* as taught in Liu. Unlike Liu and Goldenberg, Applicants' disclosure teaches and now claims a composition having a protein concentration ranging from about 0.3 mg/ml to about 0.96 mg/ml—a composition ***two magnitudes lower*** than the concentrations described in Liu and Goldenberg. This marked difference between Applicants' claims, as amended, and Liu and Goldenberg patentably distinguishes Applicants' disclosure. "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (CCPA 1970). Based on the explicit and apparent distinction between protein concentration ranges discussed above, claim 1 patentably defines over Liu in view of Goldenberg.

Sahner does not teach or suggest protein concentration of G-CSF; therefore, Sahner does not compensate for the deficiencies of Liu and Goldenberg. Thus, claim 1 and claim 20 patentably define over Liu in view of Goldenberg in further view of Sahner. Reconsideration and allowance of claims 1 and 20 are respectfully requested.

"If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious." M.P.E.P. § 2143.03 (citing *In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988)). Dependent claims 2, 3, 6-15, and 19 depend from independent claim 1,

and contain additional distinguishing features described in Applicants' disclosure. Therefore, dependent claims 2, 3, 6-15, and 19 patentably define over Liu in view of Goldenberg in further view of Sahner. Reconsideration and allowance of dependent claims 2, 3, 6-15, and 19 are respectfully requested.

II. Nonstatutory Obviousness-type Double Patenting Rejection

In addition, claims 1 – 3 and 8 – 11 were provisionally rejected for nonstatutory obviousness-type double patenting as being unpatentable over claims 1 – 10 of copending application no. 10/583,157.

Since this is a provisional rejection, the Applicants understand that it is not necessary to submit a terminal disclaimer at this time. As the Examiner notes, the first of the two cases to be allowed (either the present case or the '157 application) will not need a Terminal Disclaimer. Neither case has been allowed yet, but the present application is the earlier-filed case and appears to be further along in its prosecution. Should the '157 application ultimately be allowed before the present application, then the Applicants will submit an appropriate Terminal Disclaimer in the present case. For the present, however, the Applicants will wait to see which case advances to allowance first.

In light of the foregoing, Applicants respectfully request the Examiner reconsider the application, withdraw the rejections, and issue a notice of allowance at the earliest possible convenience.

In the event this response is not timely filed, Applicants hereby petition for the appropriate extension of time and request that the fee for the extension along with any other fees which may be due with respect to this paper be charged to our **Deposit Account No. 12-2355.**

Respectfully submitted,

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Date: February 25, 2009
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